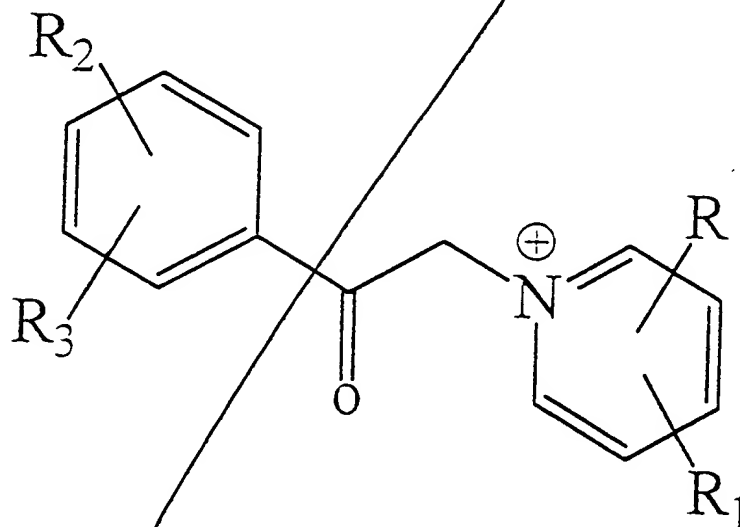


We claim:

1. An ischemia-damage mitigating compound <sup>or salt</sup> having a formula I:



I

wherein R and R<sub>1</sub> are independently hydrogen, sulfamide, carboxamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F), wherein both R and R<sub>1</sub> cannot be hydrogen, wherein R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, sulfamide, carboxamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F). <sup>and either R or R<sub>1</sub> is COOH</sup>

2. The ischemia-damage mitigating compound of claim 1 wherein R and R<sub>1</sub> are meta to each other and to the heteroatom.

~~3. The ischemia-damage mitigating compound of claim 1 wherein R is COOH.~~

~~4. The ischemia-damage mitigating compound of claim 1 wherein R<sub>1</sub> is COOH.~~

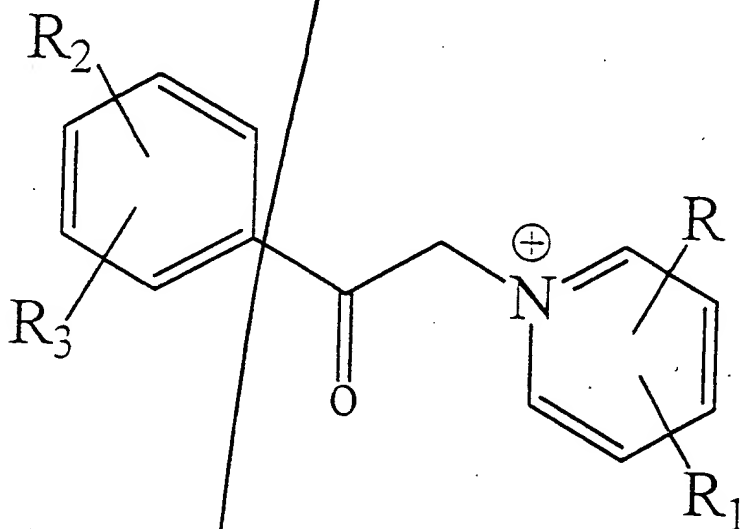
5. The ischemia-damage mitigating compound of claim 1 wherein R<sub>2</sub> and R<sub>3</sub> are both hydrogen.

6. The ischemia-damage mitigating compound of claim 1 wherein R and R<sub>1</sub> are each COOH, and R<sub>2</sub> and R<sub>3</sub> are both hydrogen.

7. The ischemia-damage mitigating compound of claim 1 wherein the compound is selected from the group consisting of 1-phenacyl-2,3-dicarboxypyridinium bromide; 1-phenacyl-2,4-dicarboxypyridinium bromide; 1-phenacyl-2,5-dicarboxypyridinium bromide (AP5); 1-

phenacyl-2,6-dicarboxypyridinium bromide; 1-phenacyl-2,3-dicarboxyimidepyrdinium bromide; 1-phenacyl-2,4-dicarboxyimidepyrdinium bromide; 1-phenacyl-2,5-dicarboxyimidepyrdinium bromide; and 1-phenacyl-2,6-dicarboxyimidepyrdinium bromide.

8. A pharmaceutical composition comprising a compound from formula I in a pharmaceutically acceptable carrier, wherein formula I comprises:



wherein R and R<sub>1</sub> are independently hydrogen, sulfamide, carboxyamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F), wherein both R and R<sub>1</sub> cannot be hydrogen, wherein R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, sulfamide, carboxyamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F).

6. 9. The pharmaceutical composition of claim 8 wherein R and R<sub>1</sub> are meta to each other and to the heteroatom.

7. 10. The pharmaceutical composition of claim 8 wherein R is COOH.

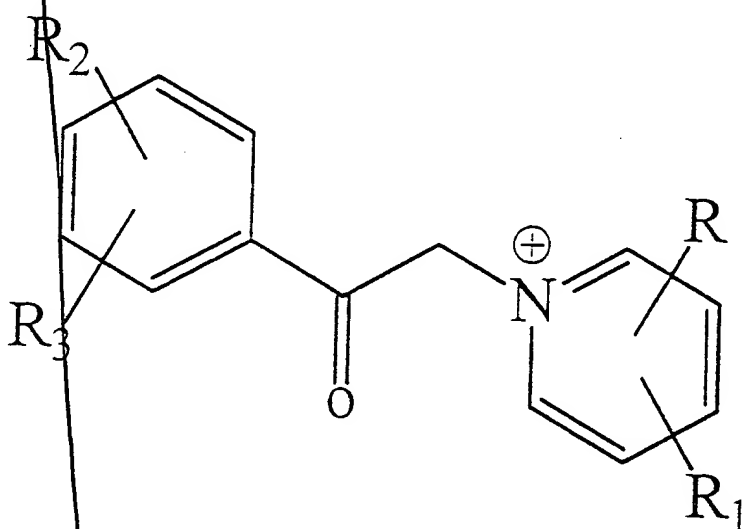
8. 11. The pharmaceutical composition of claim 8 wherein R<sub>1</sub> is COOH.

9. 12. The pharmaceutical composition of claim 8 wherein R<sub>2</sub> and R<sub>3</sub> are both hydrogen.

10. 13. The pharmaceutical composition of claim 8 wherein R and R<sub>1</sub> are each COOH, and R<sub>2</sub> and R<sub>3</sub> are both hydrogen.

14. The pharmaceutical composition of claim 8 wherein the compound is selected from the group consisting of 1-phenacyl-2,3-dicarboxypyridinium bromide; 1-phenacyl-2,4-dicarboxypyridinium bromide; 1-phenacyl-2,5-dicarboxypyridinium bromide (AP5); 1-phenacyl-2,6-dicarboxypyridinium bromide; 1-phenacyl-2,3-dicarboxyimidepyridinium bromide; 1-phenacyl-2,4-dicarboxyimidepyridinium bromide; 1-phenacyl-2,5-dicarboxyimidepyridinium bromide; and 1-phenacyl-2,6-dicarboxyimidepyridinium bromide.

15. A method for inhibiting tissue damage caused by ischemia, comprising administering an effective amount of a compound of formula I, wherein formula I comprises:



wherein R and R<sub>1</sub> are independently hydrogen, sulfamide, carboxamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F), wherein both R and R<sub>1</sub> cannot be hydrogen, wherein R<sub>2</sub> and R<sub>3</sub> are independently hydrogen, sulfamide, carboxamide, cyano, straight or branched C<sub>1-6</sub> alkyl, straight or branched C<sub>2-6</sub> alkenyl, straight or branched C<sub>1-6</sub> alkoxy, a straight chain C<sub>1-6</sub> alkyl or a straight chain C<sub>2-6</sub> alkenyl having an ether link or an ester link, toluenyl, COOH, nitrate, or halide (Br, Cl, I, F).

16. The method of claim 15 wherein R and R<sub>1</sub> are meta to each other and to the heteroatom.

17. The method of claim 15 wherein R is COOH.

18. The method of claim 15 wherein R<sub>1</sub> is COOH.

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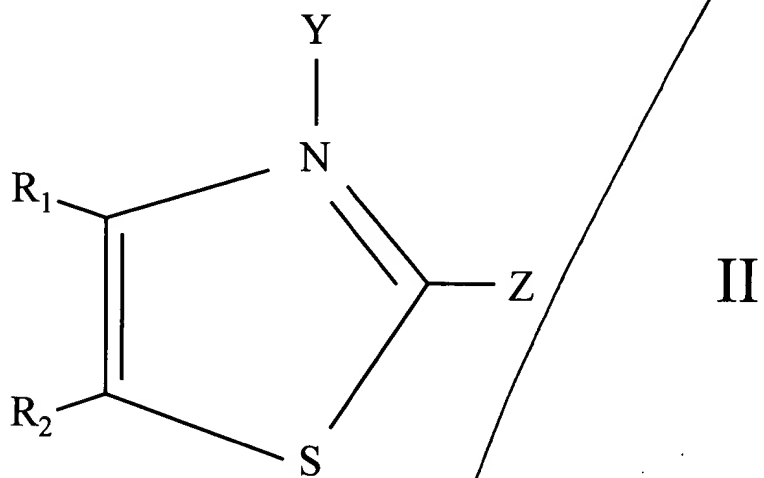
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The method of claim 15 wherein  $R_2$  and  $R_3$  are both hydrogen.

The method of claim 15 wherein  $R$  and  $R_1$  are each  $\text{COOH}$ , and  $R_2$  and  $R_3$  are both hydrogen.

21. The method of claim 15 wherein the compound is selected from the group consisting of 1-phenacyl-2,3-dicarboxypyridinium bromide; 1-phenacyl-2,4-dicarboxypyridinium bromide; 1-phenacyl-2,5-dicarboxypyridinium bromide (AP5); 1-phenacyl-2,6-dicarboxypyridinium bromide; 1-phenacyl-2,3-dicarboxyimidepyridinium bromide; 1-phenacyl-2,4-dicarboxyimidepyridinium bromide; 1-phenacyl-2,5-dicarboxyimidepyridinium bromide; and 1-phenacyl-2,6-dicarboxyimidepyridinium bromide.

22. A method for inhibiting tissue damage caused by ischemia, comprising administering an effective amount of a compound of formula II, wherein formula II comprises:



wherein  $R_1$  and  $R_2$  are independently selected from the group consisting of hydrogen, hydroxy  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy  $\text{C}_{1-6}$  alkyl, and  $R_1$  and  $R_2$  together with their ring carbons may be an aromatic fused ring; wherein  $Z$  is hydrogen or an amino group; wherein  $Y$  is hydrogen or a group of the formula  $-\text{CH}_2\text{COR}$ ; wherein  $R$  is  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy, hydroxy, amino, aryl, or  $-\text{CH}_2\text{R}_3$  wherein  $R_3$  is H,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, or  $\text{C}_{4-6}$  aryl.

23. The method of claim 22 wherein the compound of formula II is a halide (Cl, Br, F or I), tosylate, methanesulfonate or mesitylene sulfonate salt.

24. A method for treating tissue damage caused by ischemia, comprising administering an effective amount of a compound that detoxifies 3-aminopropanal.

25. The method of claim 24 wherein the tissue damage resulting from ischemia are manifest as myocardial infarction or stroke.

26. An *in vivo* screening assay comprising administering a polyamine compound or 3-aminopropanal into the brain parenchyma of a test animal by microinjection, administering a test

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compound or control agent locally or systemically, and measuring cytotoxicity in stained brain sections from the test animals.

27. An *in vitro* screening assay comprising exposing cultured glial cells or neuronal cells related cell lines to 3-aminopropanal at a concentration of from about 50 to about 1000  $\mu\text{M}$ ,  
5 adding various concentrations of test compound or control media to the cell cultures, incubated under cell culture conditions for a period of from about 5 minutes to about 20 hours, and determining the percentage of cell viability.

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